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=> index bioscience
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FULL ESTIMATED COST                                       0.42       0.42

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       AQUASCI, BIOENG, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA, CAPLUS,
       CEABA-VTB, CIN, CONFSCI, CROPB, CROPU, DDFB, DDFU, DGENE, DISSABS, DRUGB,
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69 FILES IN THE FILE LIST IN STNINDEX

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=> s (sol (2a) gel) (s) enzym##
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  10 FILES HAVE ONE OR MORE ANSWERS,   69 FILES SEARCHED IN STNINDEX

L3   QUE L2 AND (MULTIPL##### OR PLURAL#### OR ARRAY###)

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L6            7 L5 NOT PY>2003

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L6   ANSWER 1 OF 7  USPAT2 on STN
ACCESSION NUMBER:       2002:43104  USPAT2 <<LOGINID::20080306>>
TITLE:                  Biological fuel cell and methods
INVENTOR(S):            Heller, Adam, Austin, TX, United States
PATENT ASSIGNEE(S):     TheraSense, Inc., Alameda, CA, United States (U.S.
                        corporation)
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	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6531239	B2	20030311
APPLICATION INFO.:	US 2001-961621		20010924 (9)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1998-203227, filed on 30 Nov 1998, now patented, Pat. No. US 6294281		

	NUMBER	DATE
PRIORITY INFORMATION:	US 1998-89900P	19980617 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Ryan, Patrick
ASSISTANT EXAMINER: Wills, M.
LEGAL REPRESENTATIVE: Merchant & Gould P.C.
NUMBER OF CLAIMS: 16
EXEMPLARY CLAIM: 1,15,16
NUMBER OF DRAWINGS: 5 Drawing Figure(s); 1 Drawing Page(s)
LINE COUNT: 931
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A fuel cell has an anode and a cathode with anode enzyme disposed on the anode and cathode enzyme is disposed on the cathode. The anode is configured and arranged to electrooxidize an anode reductant in the presence of the anode enzyme. Likewise, the cathode is configured and arranged to electroreduce a cathode oxidant in the presence of the cathode enzyme. In addition, anode redox hydrogel may be disposed on the anode to transduce a current between the anode and the anode enzyme and cathode redox hydrogel may be disposed on the cathode to transduce a current between the cathode and the cathode enzyme.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 2 OF 7 IFIPAT COPYRIGHT 2008 IFI on STN

AN 10431277 IFIPAT;IFIUDB;IFICDB <<LOGINID::20080306>>
TITLE: SORTING AND IMMOBILIZATION SYSTEM FOR NUCLEIC ACIDS USING SYNTHETIC BINDING SYSTEMS; ELECTRONIC ARRAY FOR SOLID PHASE SYNTHESIS; KITS
INVENTOR(S): Anderson; Richard R., Encinitas, CA, US
Brucher; Christoph, Sulzbach, DE
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Kienle; Stefan, Frankfurt, DE
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Orwick; Jill, Kelkheim, DE
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Raddatz; Stefan, Wiesbaden, DE
Schneider; Eberhard, Kelkheim, DE
Schweitzer; Markus, Frankfurt am Main, DE, US
Windhab; Norbert, Hofheim am Taunus, DE
PATENT ASSIGNEE(S): Unassigned
PATENT ASSIGNEE PROBABLE: Nanogen Recognomics GmbH DE (Probable)
AGENT: O'MELVENY & MEYERS, 114 PACIFICA, SUITE 100, IRVINE, CA, 92618, US

	NUMBER	PK	DATE
PATENT INFORMATION:	US 2003175702	A1	20030918
APPLICATION INFORMATION:	US 2001-910469		20010719
FAMILY INFORMATION:	US 2003175702		20030918
	US 6893822		20050517

DOCUMENT TYPE: Utility
Patent Application - First Publication

FILE SEGMENT: CHEMICAL
APPLICATION
ENTRY DATE: Entered STN: 19 Sep 2003
Last Updated on STN: 11 Nov 2004

NUMBER OF CLAIMS: 326 29 Figure(s).
DESCRIPTION OF FIGURES:
FIG. 1: A diagrammatic representation of some preferred arrangements for linking nucleic acids (NA) to synthetic binding units (SBU,) and how such conjugates can be used for immobilization on support materials (SM) using synthetic addressing units (SAU.) FIG. 1A shows the linkage of a nucleic acid via its 3' end to the end of the SBU which points away from the support when paired with the SAU. FIG. 1B shows the linkage of a nucleic acid via its 5' end to the end of the SBU which points away from the support. FIG. 1C shows the linkage of a nucleic acid via its 5' end to the end of the binding unit which points towards the support. FIG. 1D shows the linkage of a nucleic acid via its 5' end to a position in the center of the binding unit. An example of this type of linkage would be a the conjugation of a tryptamine base linker in a pRNA with an aldehyde on the end of a nucleic acid.
FIG. 2: An illustration of some preferred linkage arrangements and spacers for use with nucleic acids and pRNA synthetic binding units. R1=H, OH, OMe, Me; R2=H, OH, OMe; L=(CH2)n; CH2CH2-(-O-CH2-CH2-)m-O-CH2-CH2. CH2-CH2-CH2-(-O-CH2-CH2-CH2-)q-O -CH2-CH2-CH2;Ba=heterocyclic base (C, T, U, G, A, etc.)A: Linkage of the 4' end of a pyranosyl building block of a SBU to the 3' end of a nucleic acid directly through a phosphate. B: Linkage of the 4' end of a pyranosyl building block of an SBU to the 5' end of a nucleic acid directly through a phosphate. C: Linkage of the 2' end of a pyranosyl building block of an SBU to the 5' end of a nucleic acid directly through a phosphate. D: Linkage of the 4' end of a pyranosyl building block of an SBU to the 3' end of a nucleic acid via a linker (L) . E: Linkage of the 4' end of a pyranosyl building block of an SBU to the 5' end of a nucleic acid via a linker (L). F: Linkage of the 2' end of a pyranosyl building block of an SBU to the 5' end of a nucleic acid via a linker (L).
FIG. 3: A diagrammatic representation of the three dimensional structural difference between nucleic acids and the preferred synthetic binding systems for use in the invention. FIG. 3A shows the helical form of nucleic acid duplexes on the basis of a B-DNA helix. FIG. 3B shows the non-helical nature of synthetic binding systems such as pRNA, pDNA, and CNA. FIG. 3C shows the example of a binding unit (SBU) 102a and address unit (SAU) 102b. NA=nucleic acid; SM=support material; in this example, the address 102b is immobilized and 102a is conjugated with the nucleic acid (NA) via a linker. The inter-strand base stacking interactions (stacks) are shown using the example of purine-purine base stacking interactions (Pu-Pu stack) and of purine-pyrimidine base stacking interactions (Pu-Py stack). 0 stack means the absence of such a base stacking interaction. The pyrimidine-purine stacks possible in principle are not present in this specific example.
FIG. 4: An exemplary illustration of some embodiments of pRNA binding addresses and conjugates. 4A shows a synthetic address unit (SAU) having a 4' end biotin (BIO) for immobilization on support materials coated with streptavidin, 4B shows a synthetic address unit (SAU) with a tetrahydrazide (4HY) moiety for immobilization on active ester surfaces, and 4C shows a conjugate of a pRNA unit (SBU) and a DNA (NA).
FIG. 5: An illustration of the conjugation of a DNA having a 3' terminal ribonucleotide (NA) with a vicinal diol, and a 2' Cy3labeled and 4' monohydrazide-modified pRNA (L HY pRNA) to give a conjugate (C) as described in Example 1.4.
FIG. 6: An illustration of the conjugation of a 3' glycerylmodified DNA (Gly NA) via the oxidized aldehyde DNA (OB NA) intermediate with a 2' Cy3-labeled and 4' monohydrazidemodified pRNA (L HY pRNA) to give a conjugate (C) as described in Example 1.5.
FIG. 7: FIG. 7A illustrates the immobilization of nucleic acids (NA) which are

linked via a branching site (BS) to a plurality of identical binding units for the immobilization on support materials (SM). FIG. 7B shows the use of two different synthetic binding systems (SAU1 and SBU1 and also SAU2 and SBU2) for the immobilization of a nucleic acid through a branching structure. An advantage of these structures in the increased, additive binding energy immobilizing the nucleic acid.

FIG. 8: An illustrative conjugate in which a nucleic acid (NA) is linked via a branching site (BS), or a branching moiety W, to a plurality of identical binding units (SBU).

FIG. 9: A diagram of some possible embodiments of labeled synthetic binding addresses and synthetic binding units or conjugates. 9A shows a conjugate of a nucleic acid (NA) and synthetic binding unit (SBU) with a marker at the end of the binding unit, as through the end phosphate (SM=support material) . B depicts the arrangement for the marker group (M) to be located at any position in the conjugate, for example through the use of a base-labeling moiety. C shows the use of a labeled synthetic binding address. D shows the joint use of two marker groups (M1 and M2) which have been adjusted to one another and give a signal in the form of fluorescence quenching or fluorescence resonance energy transfer (FRET) when a conjugate binds to the synthetic binding address.

FIG. 10: An illustration of an additional embodiment in which a ***plurality*** of different molecular species or nucleic acids (NA1 and NA2) are immobilized next to one another on the same array position, or capture site. This can be achieved, as depicted in 10A, by fixing two different SAU's to one site to form two different binding systems (SBS) at one ***array*** location (L). Or, as depicted in B, the same effect may be achieved by using the same binding system (SBS), and using conjugates of different nucleic acids (NA 1 and NA 2) with the same SBU.

FIG. 11: An illustration of the use of synthetic binding addresses and conjugates of synthetic binding units with nucleic acids for the co

DESCRIPTION OF FIGURES:

nstruction of arrays on support materials (SM). Figure A shows an embodiment in which different nucleic acids (NA 1, NA 2, NA 3, . . .) are immobilized on different locations (L) of the support material using different binding units (SBU 1, SBU 2, SBU 3, . . .) and different address units (SAU 1, SAU 2, SAU 3 . . .). The SAUs of the locations are, for example, simply spotted on passive arrays, or may be electronically addressed to capture sites above electrodes in the case of active electronic arrays. A characteristic of the embodiment is that each array location carries a distinctive binding address. Although this is illustrated here as a separate SAU for each SP, the distinctive addresses may as easily be formed by mixtures of SAU's (e.g., SAU 1&2 at L 1, SAU 3&4 at L 2, etc.). FIG. 11B shows that for immobilizing a nucleic acid (NA) on a support material (SM) SBU (here pRNA) and SAU (here CNA) need not belong to one molecular class. Any sterically compatible molecules which form a stable and selective immobilization upon recognition are suitable for use in these formats. FIG. 12: A diagram showing an embodiment of the method for using synthetic address units and conjugates of synthetic binding units with nucleic acids to construct arrays on support materials. As illustrated, individual array positions can specifically and independently of one another be addressed by utilizing ***array*** surfaces with individually activatable locations, such as, for example, active electronic arrays. Initially, N different binding addresses (a, b, c, . . . N) are fixed to the surface of the support material. In this step, synthetic address units are affixed to groups of M-number of active sites utilizing the same immobilization method (e.g., biotin-streptavidin interaction, or hydrazide-active ester chemistry) in a number of steps (e.g., spotting or electronic addressing.) The immobilization is preferably carried out so that identical synthetic binding units are deposited either in rows or columns, although other geometries (e.g., squares, crosses, circles, or even randomly chosen groups of sites) may be used. Thus an ***array*** of N different binding addresses is obtained, in which each unit appears in M-fold repetition (FIG. 12A). In the following steps, conjugates of

nucleic acids and synthetic binding units are contacted with the array generated previously. Although this can be carried out either individually using individual SBU/NA conjugates, sets of different SBU/NA conjugates are advantageously used to immobilize up to N different SBU-encoded nucleic acids in one step. It is important that the method can only be used in those ***arrays*** in which individual array positions can be activated specifically and independently of one another, e.g., in active electronic ***arrays.*** The activated positions in each step create a condition which is favorable to the binding of the SBUs with the attached SAUs. In the preferred embodiment, mixtures of N different conjugates (or SBU-encoded groups of conjugates) are addressed to N array positions, and this addressing can be carried out sequentially or parallel to all N positions. These sets may contain N different nucleic acids (v, w, x, y, . . . N) all of which are conjugated with an individual synthetic binding unit (a', b', c', . . . N). The specific recognition of the fixed synthetic address unit by the binding units leads to only that type of nucleic acid, which has been conjugated with the corresponding synthetic binding unit complementary to the fixed binding unit, being immobilized on each array position. In other words, the set of conjugates is sorted to specific locations. Thus, in a single process step N different conjugates (a'-v1, b'-w1, c'-x1, d'-y1, . . . N) are immobilized. Although a row/column addressing scheme is shown here, other geometries are possible. After the binding of each set of conjugates to each activated set of locations, the unbound conjugates are removed. This procedure can then be repeated using a new second set of conjugates (a'-v2, b'-w2, c'x2, d'-y2, . . . N). In each repetition, again up to N conjugates are immobilized in parallel. Thus, after M repetitions, W different conjugates are immobilized on the array, with W=N x M.

FIG. 13: shows further embodiments for using synthetic binding systems for the immobilization of nucleic acids on support material. FIG. 13A shows an example of an array of N different address units. In additional embodiments, one may wish to attach individual address units two or more times to different ***array*** positions for duplicate addressing at those positions. This embodiment is typical for passive arrays, although it may be utilized in active location array systems as well. FIG. 13B shows, by way of example, an embodiment for using synthetic binding systems for generating ***arrays*** of nucleic acids for the analyses of different samples of nucleic acids, as can be applied to gene expression studies. Here, different times, stages or populations of nucleic acids, for example particular gene probe sequences which have been hybridized to different samples, are compared with one another on an array. Here, by way of example, the immobilization of three times T1, T2, T3 of various nucleic acid sequences (genes; S1, S2, S3, . . .) is depicted. Initially, an array of fixed synthetic address units is prepared. Times to be compared may thereafter by differentiated by particular sets of SBU's conjugated with the set of nucleic acid sequences to be monitored. The times to be compared of may be allowed to associate with the SAU's either simultaneously or sequentially. The specific recognition of synthetic address units by the synthetic binding units immobilizes on each array position only the conjugate specifically belonging to the position, thus locating the sample nucleic acids hybridized according to the SBU utilized. An advantage to simultaneous addressing of several samples at one once is that variability in hybridization conditions caused by the individual incubation of the samples with the array may be avoided, allowing for more rigorous and quantitative comparison of the results. In addition, the ability to assay multiple samples in one cycle saves time compared with individual addressing, or hybridization with separate arrays.

FIG. 14: A graph of the result of a surface plasmon resonance experiment (SPR) in which 14 synthetic address units are contacted with 14 synthetic binding units. The signal increasing from the baseline upward indicates binding. As expected, all address units bind to the in each case corresponding specific binding unit (e.g. 102a to 102b). Some address units and binding units,

however, show some degree of cross-association with units which are not exactly complementary (e.g. 105b with 110a). Sets of binding units in which such cross-association reactions are substantially reduced are said to be "orthogonal". Although suitable for some uses, non-orthogonal units should not be used together in one set of synthetic binding systems when strict sorting according to the addressing units is desired.

FIG. 15: A photograph and chart of the specific association of fluorescently labeled binding units to synthetic address units attached to the surface of an active electronic array. The strongest fluorescence signals are all on a diagonal with the specific SBU-SAU pairs, as expected.

FIG. 16: A chart of the association of conjugates of nucleic acids (C) and pRNA/SBUs with pRNA/SAU's attached to the surface of the SPR chip, also demonstrating specific binding between the coordinating pairs. 4' biotinylated 102b, 103b, 104b, and 105b, prepared as in Example 2.1, were immobilized on the Sensor Chip channels as described in Example 8. Conjugates IL4RP102a, IL4RP103a, and IL4RP104a, prepared as in Example 1.1, were then sequentially assayed for binding to the SAUs in the channels.

FIG. 17: A chart of the immobilization of a conjugate IL4RP102a (Example 1.1) by biotinylated synthetic address unit 102b (Example 2.1) on an SPR chip and subsequent hybridization of the nucleic acid part of the conjugate with three complementary DNA fragments. IL4RP102C1 was a complementary sequence to all but the 5' three nucleotides of the NA portion of IL4RP102a, IL4RP102C2 was a full complementary sequence, and IL4RP102C3 was a full complementary sequence plus three nucleotides. This experiment also illustrates the ability of the attached SAUs to be utilized repeatedly by simply stripping of the bound SBU conjugates with a mild base solution (e.g.10 mM NaOH).

FIG. 18: A diagram of the setup and negative photographs of the results of the Example 5.2. Mixtures of cy3 labeled and one unlabeled synthetic binding unit-nucleic acid conjugates (SBUNA) are addressed on an active electronic ***array.*** Each conjugate is immobilized to the position with the matching synthetic address unit (SAU). The fluorescence measured is displayed as a diagram and a chip image.

FIG. 19: 19A: a diagram of the use of a conjugate (C) of a synthetic binding unit (SBU) and a nucleic acid section (NA) as the substrate (primer) for a polymerase (E) which carries out a nucleic acid template-dependent synthesis, a first step in amplification reactions. 19B: a diagram of the use of a conjugate (C) of a synthetic binding unit (SBU) and a nucleic acid section (NA) as the substrate of a single-strand ligase (E) which links the conjugate to a nucleic acid. Although shown with a relatively long NA section on the conjugate, ligase reactions may utilize conjugates with just a single nucleic acid residue.

DESCRIPTION OF FIGURES:

FIGS. 20A & B: Diagrams of the use of a conjugate (C) of a synthetic binding unit (SBU) and a nucleic acid section (NA) as substrates for nuclease reactions. A: The conjugate and a target nucleic acid are cleaved in a restriction endonuclease (E) reaction. This reaction can be especially useful when coupled with fluorescent energy transfer labeling, as shown here. The emissions of a fluorophore moiety (F) may be masked by placing a quencher moiety (Q) on the same conjugate. After cleavage, emissions of the fluorophore are no longer absorbed by the quencher, and become visible. The progress of this reaction may be quantified dynamically (real time), or after completion, in order to quantify the amount of the target in the sample. B: The target nucleic acid is selectively degraded by an endonuclease (E) when hybridized to the conjugate nucleic acid portion. This can be especially useful for degrading RNA target nucleic acids with double-stranded specific RNAses, such as RNAse H.

FIG. 21: An illustration of representative pRNA-DNA conjugates. A: a NA/SBU conjugate of a pRNA (SBU) with 2'-OMe-RNA (NA) and 5' phosphate (P) (a suitable substrate for a ligase reaction); the conjugate additionally carries a fluorescence dye at its 3' end. B: a NA/SBU conjugate of a pRNA unit (SBU) and a DNA (NA) with free 3' end (a suitable substrate for a polymerase or restriction endonuclease reaction.)

FIG. 22: A: a photograph of an agarose gel showing the formation of specific of

amplification products in a PCR reaction using pRNA-DNA conjugates as primers. For comparison, mixtures using standard DNA primers were also applied (see Example 2). B: another photograph of an agarose gel showing the result of a large-scale PCR reaction using NA/SBU conjugates as primers (see Example 3).
FIG. 23: A photograph of a 10% polyacrylamide gel showing the products of ligation of a fluorescence-labeled conjugate of pRNA and 2'-OMe-RNA with a target RNA, under both UV shadowing and fluorescence imaging. Due to its short length, the free unligated NA/SBU conjugate is not displayed on the gel (see Example 4). The Lanes of the gels are as follows:
FIG. 24 An illustration showing, schematically, an array of SAU on locations (L) to which a series of distinct SDA primers have been addressed via the interaction between the SAU and SAU.
FIG. 25: An illustration showing that that two different primers can be addressed using a single SBS by using a branched linker to attach the primers to one SBU.
FIG. 26: An illustration showing that shows the general architecture of the SBU anchored SDA construct. The SDA primers contain a restriction site template and a region complementary to the target DNA. The bumper primers are sequences complementary to a region of the target DNA upstream of where the SDA primer binds. The bumper primers form the initiation sites for the polymerase and lead to the initial strand displacement of the target nucleic acid from the extended primer.
FIGS. 27A and 27B: An illustration of the initiation steps for SBU-anchored SDA (phase 1): Copying of the target sequence onto the SBU-anchored SDA primer, Displacement of the genomic DNA by extension from bumper primer 1, Activation of the restriction site, and Generation of displaced S1 strands.
FIG. 27C: An illustration of the linear amplification reactions of SBU anchored SDA (phase 2): The generation of a single stranded anchored amplicon for every Phase 1 displaced strand captured.
FIGS. 27D and 27E: An illustration of the exponential amplification reactions of SBU anchored SDA (phase 3): Activation of restriction sites in both anchored amplicons, Generation of displaced S1 and S2 strands, and exponential amplification via bridging and capture.
FIG. 28: An illustration of the specific addressing experiment described in Example 5.3. The first two columns of addressed, immobilized nucleic acid/SBU conjugates and hybridized labeled nucleic acids are illustrated by the small figures under the headings "Column 1" and "Column 2". The green fluorescent signal is shown to the left, and the red fluorescent signal is shown to the right, for each of the two columns. Note that this experiment demonstrates that there is no significant hybridization of the complementary sequences to non-activated locations within the array, allowing one to effectively isolate hybridization reactions using the same sequences from different samples at different locations. !

AB The present invention relates to conjugates of synthetic binding units and nucleic acids. The present invention also relates to methods for sorting and immobilizing nucleic acids on support materials using such conjugates by specific molecular addressing of the nucleic acids mediated by the synthetic binding systems. Particularly, the present invention also relates to novel methods of utilizing conjugates of synthetic binding units and nucleic acids to in active electronic array systems to produce novel array constructs from the conjugates, and the use of such constructs in various nucleic acid assay formats. In addition, the present invention relates to various novel forms of such conjugates, improved methods of making solid phase synthesized conjugates, and improved methods of conjugating pre-synthesized synthetic binding units and nucleic acids. The present invention also relates to the use of conjugates of synthetic binding units and nucleic acids as substrates for various enzymatic reactions, including nucleic acid amplification reactions.

CLMN 326 29 Figure(s).
FIG. 1: A diagrammatic representation of some preferred arrangements for

linking nucleic acids (NA) to synthetic binding units (SBU,) and how such conjugates can be used for immobilization on support materials (SM) using synthetic addressing units (SAU.) FIG. 1A shows the linkage of a nucleic acid via its 3' end to the end of the SBU which points away from the support when paired with the SAU. FIG. 1B shows the linkage of a nucleic acid via its 5' end to the end of the SBU which points away from the support. FIG. 1C shows the linkage of a nucleic acid via its 5' end to the end of the binding unit which points towards the support. FIG. 1D shows the linkage of a nucleic acid via its 5' end to a position in the center of the binding unit. An example of this type of linkage would be a the conjugation of a tryptamine base linker in a pRNA with an aldehyde on the end of a nucleic acid.

FIG. 2: An illustration of some preferred linkage arrangements and spacers for use with nucleic acids and pRNA synthetic binding units. R1=H, OH, OMe, Me; R2=H, OH, OMe; L=(CH2)n; CH2CH2-(-O-CH2-CH2-)m-O-CH2-CH2. CH2-CH2-CH2-(-O-CH2-CH2-CH2-)q-O -CH2-CH2-CH2;Ba=heterocyclic base (C, T, U, G, A, etc.)A: Linkage of the 4' end of a pyranosyl building block of a SBU to the 3' end of a nucleic acid directly through a phosphate. B: Linkage of the 4' end of a pyranosyl building block of an SBU to the 5' end of a nucleic acid directly through a phosphate. C: Linkage of the 2' end of a pyranosyl building block of an SBU to the 5' end of a nucleic acid directly through a phosphate. D: Linkage of the 4' end of a pyranosyl building block of an SBU to the 3' end of a nucleic acid via a linker (L) . E: Linkage of the 4' end of a pyranosyl building block of an SBU to the 5' end of a nucleic acid via a linker (L). F: Linkage of the 2' end of a pyranosyl building block of an SBU to the 5' end of a nucleic acid via a linker (L).

FIG. 3: A diagrammatic representation of the three dimensional structural difference between nucleic acids and the preferred synthetic binding systems for use in the invention. FIG. 3A shows the helical form of nucleic acid duplexes on the basis of a B-DNA helix. FIG. 3B shows the non-helical nature of synthetic binding systems such as pRNA, pDNA, and CNA. FIG. 3C shows the example of a binding unit (SBU) 102a and address unit (SAU) 102b. NA=nucleic acid; SM=support material; in this example, the address 102b is immobilized and 102a is conjugated with the nucleic acid (NA) via a linker. The inter-strand base stacking interactions (stacks) are shown using the example of purine-purine base stacking interactions (Pu-Pu stack) and of purine-pyrimidine base stacking interactions (Pu-Py stack). 0 stack means the absence of such a base stacking interaction. The pyrimidine-purine stacks possible in principle are not present in this specific example.

FIG. 4: An exemplary illustration of some embodiments of pRNA binding addresses and conjugates. 4A shows a synthetic address unit (SAU) having a 4' end biotin (BIO) for immobilization on support materials coated with streptavidin, 4B shows a synthetic address unit (SAU) with a tetrahydrazide (4HY) moiety for immobilization on active ester surfaces, and 4C shows a conjugate of a pRNA unit (SBU) and a DNA (NA).

FIG. 5: An illustration of the conjugation of a DNA having a 3' terminal ribonucleotide (NA) with a vicinal diol, and a 2' Cy3labeled and 4' monohydrazide-modified pRNA (L HY pRNA) to give a conjugate (C) as described in Example 1.4.

FIG. 6: An illustration of the conjugation of a 3' glycerylmodified DNA (Gly NA) via the oxidized aldehyde DNA (OB NA) intermediate with a 2' Cy3-labeled and 4' monohydrazidemodified pRNA (L HY pRNA) to give a conjugate (C) as described in Example 1.5.

FIG. 7: FIG. 7A illustrates the immobilization of nucleic acids (NA) which are linked via a branching site (BS) to a plurality of identical binding units for the immobilization on support materials (SM). FIG. 7B shows the use of two different synthetic binding systems (SAU1 and SBU1 and also SAU2 and SBU2) for the immobilization of a nucleic acid through a branching structure. An advantage of these structures in

the increased, additive binding energy immobilizing the nucleic acid.

FIG. 8: An illustrative conjugate in which a nucleic acid (NA) is linked via a branching site (BS), or a branching moiety W, to a plurality of identical binding units (SBU).

FIG. 9: A diagram of some possible embodiments of labeled synthetic binding addresses and synthetic binding units or conjugates. 9A shows a conjugate of a nucleic acid (NA) and synthetic binding unit (SBU) with a marker at the end of the binding unit, as through the end phosphate (SM=support material) . B depicts the arrangement for the marker group (M) to be located at any position in the conjugate, for example through the use of a base-labeling moiety. C shows the use of a labeled synthetic binding address. D shows the joint use of two marker groups (M1 and M2) which have been adjusted to one another and give a signal in the form of fluorescence quenching or fluorescence resonance energy transfer (FRET) when a conjugate binds to the synthetic binding address.

FIG. 10: An illustration of an additional embodiment in which a plurality of different molecular species or nucleic acids (NA1 and NA2) are immobilized next to one another on the same array position, or capture site. This can be achieved, as depicted in 10A, by fixing two different SAU's to one site to form two different binding systems (SBS) at one array location (L). Or, as depicted in B, the same effect may be achieved by using the same binding system (SBS), and using conjugates of different nucleic acids (NA 1 and NA 2) with the same SBU.

FIG. 11: An illustration of the use of synthetic binding addresses and conjugates of synthetic binding units with nucleic acids for the co nstruction of arrays on support materials (SM). Figure A shows an embodiment in which different nucleic acids (NA 1, NA 2, NA 3, . . .) are immobilized on different locations (L) of the support material using different binding units (SBU 1, SBU 2, SBU 3, . . .) and different address units (SAU 1, SAU 2, SAU 3 . . .). The SAUs of the locations are, for example, simply spotted on passive arrays, or may be electronically addressed to capture sites above electrodes in the case of active electronic arrays. A characteristic of the embodiment is that each array location carries a distinctive binding address. Although this is illustrated here as a separate SAU for each SP, the distinctive addresses may as easily be formed by mixtures of SAU's (e.g., SAU 1&2 at L 1, SAU 3&4 at L 2, etc.). FIG. 11B shows that for immobilizing a nucleic acid (NA) on a support material (SM) SBU (here pRNA) and SAU (here CNA) need not belong to one molecular class. Any sterically compatible molecules which form a stable and selective immobilization upon recognition are suitable for use in these formats.

FIG. 12: A diagram showing an embodiment of the method for using synthetic address units and conjugates of synthetic binding units with nucleic acids to construct arrays on support materials. As illustrated, individual array positions can specifically and independently of one another be addressed by utilizing array surfaces with individually activatable locations, such as, for example, active electronic arrays. Initially, N different binding addresses (a, b, c, . . . N) are fixed to the surface of the support material. In this step, synthetic address units are affixed to groups of M-number of active sites utilizing the same immobilization method (e.g., biotin-streptavidin interaction, or hydrazide-active ester chemistry) in a number of steps (e.g., spotting or electronic addressing.) The immobilization is preferably carried out so that identical synthetic binding units are deposited either in rows or columns, although other geometries (e.g., squares, crosses, circles, or even randomly chosen groups of sites) may be used. Thus an array of N different binding addresses is obtained, in which each unit appears in M-fold repetition (FIG. 12A). In the following steps, conjugates of nucleic acids and synthetic binding units are contacted with the array

generated previously. Although this can be carried out either individually using individual SBU/NA conjugates, sets of different SBU/NA conjugates are advantageously used to immobilize up to N different SBU-encoded nucleic acids in one step. It is important that the method can only be used in those arrays in which individual array positions can be activated specifically and independently of one another, e.g., in active electronic arrays. The activated positions in each step create a condition which is favorable to the binding of the SBUs with the attached SAUs. In the preferred embodiment, mixtures of N different conjugates (or SBU-encoded groups of conjugates) are addressed to N array positions, and this addressing can be carried out sequentially or parallel to all N positions. These sets may contain N different nucleic acids (v, w, x, y, . . . N) all of which are conjugated with an individual synthetic binding unit (a', b', c', . . . N). The specific recognition of the fixed synthetic address unit by the binding units leads to only that type of nucleic acid, which has been conjugated with the corresponding synthetic binding unit complementary to the fixed binding unit, being immobilized on each array position. In other words, the set of conjugates is sorted to specific locations. Thus, in a single process step N different conjugates (a'-v1, b'-w1, c'-x1, d'-y1, . . . N) are immobilized. Although a row/column addressing scheme is shown here, other geometries are possible. After the binding of each set of conjugates to each activated set of locations, the unbound conjugates are removed. This procedure can then be repeated using a new second set of conjugates (a'-v2, b'-w2, c'x2, d'-y2, . . . N). In each repetition, again up to N conjugates are immobilized in parallel. Thus, after M repetitions, W different conjugates are immobilized on the array, with W=N x M.

FIG. 13: shows further embodiments for using synthetic binding systems for the immobilization of nucleic acids on support material. FIG. 13A shows an example of an array of N different address units. In additional embodiments, one may wish to attach individual address units two or more times to different array positions for duplicate addressing at those positions. This embodiment is typical for passive arrays, although it may be utilized in active location array systems as well. FIG. 13B shows, by way of example, an embodiment for using synthetic binding systems for generating arrays of nucleic acids for the analyses of different samples of nucleic acids, as can be applied to gene expression studies. Here, different times, stages or populations of nucleic acids, for example particular gene probe sequences which have been hybridized to different samples, are compared with one another on an array. Here, by way of example, the immobilization of three times T1, T2, T3 of various nucleic acid sequences (genes; S1, S2, S3, . . .) is depicted. Initially, an array of fixed synthetic address units is prepared. Times to be compared may thereafter by differentiated by particular sets of SBU's conjugated with the set of nucleic acid sequences to be monitored. The times to be compared of may be allowed to associate with the SAU's either simultaneously or sequentially. The specific recognition of synthetic address units by the synthetic binding units immobilizes on each array position only the conjugate specifically belonging to the position, thus locating the sample nucleic acids hybridized according to the SBU utilized. An advantage to simultaneous addressing of several samples at one once is that variability in hybridization conditions caused by the individual incubation of the samples with the array may be avoided, allowing for more rigorous and quantitative comparison of the results. In addition, the ability to assay multiple samples in one cycle saves time compared with individual addressing, or hybridization with separate arrays.

FIG. 14: A graph of the result of a surface plasmon resonance experiment

(SPR) in which 14 synthetic address units are contacted with 14 synthetic binding units. The signal increasing from the baseline upward indicates binding. As expected, all address units bind to the in each case corresponding specific binding unit (e.g. 102a to 102b). Some address units and binding units, however, show some degree of cross-association with units which are not exactly complementary (e.g. 105b with 110a). Sets of binding units in which such cross-association reactions are substantially reduced are said to be "orthogonal". Although suitable for some uses, non-orthogonal units should not be used together in one set of synthetic binding systems when strict sorting according to the addressing units is desired.

FIG. 15: A photograph and chart of the specific association of fluorescently labeled binding units to synthetic address units attached to the surface of an active electronic array. The strongest fluorescence signals are all on a diagonal with the specific SBU-SAU pairs, as expected.

FIG. 16: A chart of the association of conjugates of nucleic acids (C) and pRNA/SBUs with pRNA/SAU's attached to the surface of the SPR chip, also demonstrating specific binding between the coordinating pairs. 4' biotinylated 102b, 103b, 104b, and 105b, prepared as in Example 2.1, were immobilized on the Sensor Chip channels as described in Example 8. Conjugates IL4RP102a, IL4RP103a, and IL4RP104a, prepared as in Example 1.1, were then sequentially assayed for binding to the SAUs in the channels.

FIG. 17: A chart of the immobilization of a conjugate IL4RP102a (Example 1.1) by biotinylated synthetic address unit 102b (Example 2.1) on an SPR chip and subsequent hybridization of the nucleic acid part of the conjugate with three complementary DNA fragments. IL4RP102C1 was a complementary sequence to all but the 5' three nucleotides of the NA portion of IL4RP102a, IL4RP102C2 was a full complementary sequence, and IL4RP102C3 was a full complementary sequence plus three nucleotides. This experiment also illustrates the ability of the attached SAUs to be utilized repeatedly by simply stripping of the bound SBU conjugates with a mild base solution (e.g.10 mM NaOH).

FIG. 18: A diagram of the setup and negative photographs of the results of the Example 5.2. Mixtures of cy3 labeled and one unlabeled synthetic binding unit-nucleic acid conjugates (SBUNA) are addressed on an active electronic array. Each conjugate is immobilized to the position with the matching synthetic address unit (SAU). The fluorescence measured is displayed as a diagram and a chip image.

FIG. 19: 19A: a diagram of the use of a conjugate (C) of a synthetic binding unit (SBU) and a nucleic acid section (NA) as the substrate (primer) for a polymerase (E) which carries out a nucleic acid template-dependent synthesis, a first step in amplification reactions. 19B: a diagram of the use of a conjugate (C) of a synthetic binding unit (SBU) and a nucleic acid section (NA) as the substrate of a single-strand ligase (E) which links the conjugate to a nucleic acid. Although shown with a relatively long NA section on the conjugate, ligase reactions may utilize conjugates with just a single nucleic acid residue.

FIGS. 20A & B: Diagrams of the use of a conjugate (C) of a synthetic binding unit (SBU) and a nucleic acid section (NA) as substrates for nuclease reactions. A: The conjugate and a target nucleic acid are cleaved in a restriction endonuclease (E) reaction. This reaction can be especially useful when coupled with fluorescent energy transfer labeling, as shown here. The emissions of a fluorophore moiety (F) may be masked by placing a quencher moiety (Q) on the same conjugate. After cleavage, emissions of the fluorophore are no longer absorbed by the quencher, and become visible. The progress of this reaction may be quantified dynamically (real time), or after completion, in order to quantify the amount of the target in the sample. B: The target nucleic acid is selectively degraded by an endonuclease (E) when hybridized to the

conjugate nucleic acid portion. This can be especially useful for degrading RNA target nucleic acids with double-stranded specific RNAses, such as RNAse H.

FIG. 21: An illustration of representative pRNA-DNA conjugates. A: a NA/SBU conjugate of a pRNA (SBU) with 2'-OMe-RNA (NA) and 5' phosphate (P) (a suitable substrate for a ligase reaction); the conjugate additionally carries a fluorescence dye at its 3' end. B: a NA/SBU conjugate of a pRNA unit (SBU) and a DNA (NA) with free 3' end (a suitable substrate for a polymerase or restriction endonuclease reaction.)

FIG. 22: A: a photograph of an agarose gel showing the formation of specific of amplification products in a PCR reaction using pRNA-DNA conjugates as primers. For comparison, mixtures using standard DNA primers were also applied (see Example 2). B: another photograph of an agarose gel showing the result of a large-scale PCR reaction using NA/SBU conjugates as primers (see Example 3).

FIG. 23: A photograph of a 10% polyacrylamide gel showing the products of ligation of a fluorescence-labeled conjugate of pRNA and 2'-OMe-RNA with a target RNA, under both UV shadowing and fluorescence imaging. Due to its short length, the free unligated NA/SBU conjugate is not displayed on the gel (see Example 4). The Lanes of the gels are as follows:

FIG. 24 An illustration showing, schematically, an array of SAU on locations (L) to which a series of distinct SDA primers have been addressed via the interaction between the SAU and SAU.

FIG. 25: An illustration showing that that two different primers can be addressed using a single SBS by using a branched linker to attach the primers to one SBU.

FIG. 26: An illustration showing that shows the general architecture of the SBU anchored SDA construct. The SDA primers contain a restriction site template and a region complementary to the target DNA. The bumper primers are sequences complementary to a region of the target DNA upstream of where the SDA primer binds. The bumper primers form the initiation sites for the polymerase and lead to the initial strand displacement of the target nucleic acid from the extended primer.

FIGS. 27A and 27B: An illustration of the initiation steps for SBU-anchored SDA (phase 1): Copying of the target sequence onto the SBU-anchored SDA primer, Displacement of the genomic DNA by extension from bumper primer 1, Activation of the restriction site, and Generation of displaced S1 strands.

FIG. 27C: An illustration of the linear amplification reactions of SBU anchored SDA (phase 2): The generation of a single stranded anchored amplicon for every Phase 1 displaced strand captured.

FIGS. 27D and 27E: An illustration of the exponential amplification reactions of SBU anchored SDA (phase 3): Activation of restriction sites in both anchored amplicons, Generation of displaced S1 and S2 strands, and exponential amplification via bridging and capture.

FIG. 28: An illustration of the specific addressing experiment described in Example 5.3. The first two columns of addressed, immobilized nucleic acid/SBU conjugates and hybridized labeled nucleic acids are illustrated by the small figures under the headings "Column 1" and "Column 2". The green fluorescent signal is shown to the left, and the red fluorescent signal is shown to the right, for each of the two columns. Note that this experiment demonstrates that there is no significant hybridization of the complementary sequences to non-activated locations within the array, allowing one to effectively isolate hybridization reactions using the same sequences from different samples at different locations. !

L6 ANSWER 3 OF 7 IFIPAT COPYRIGHT 2008 IFI on STN
AN 03058149 IFIPAT;IFIUDB;IFICDB <<LOGINID::20080306>>
TITLE: DOPED SOL-GEL GLASSES FOR

OBTAINING CHEMICAL INTERACTIONS; USEFUL AS ANALYTICAL TEST, CHROMATOGRAPHIC MEDIUM, SENSOR, CATALYST OR BIOCATALYST, ELECTRODE OR ENZYME ELECTRODE, AND OTHER DETECTION DEVICES; CELL-FREE BIOLOGICAL DOPANT

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PRIMARY EXAMINER: Lovering, Richard D

AGENT: Lowe Hauptman Gopstein Gilman & Berner

	NUMBER	PK	DATE
PATENT INFORMATION:	US 5824526	A	19981020
	(CITED IN 002 LATER PATENTS)		
APPLICATION INFORMATION:	US 1996-667746		19960621
EXPIRATION DATE:	8 Jan 2011		

	APPLN. NUMBER	DATE	GRANTED PATENT NO. OR STATUS
CONTINUATION OF:	US 1992-937259	19920831	ABANDONED
CONTINUATION OF:	US 1994-266441	19940628	5650311
DIVISION OF:	US 1991-637873	19910108	5300564

	NUMBER	DATE
PRIORITY APPLN. INFO.:	IL 1990-93134	19900123
FAMILY INFORMATION:	US 5824526	19981020
	US 5650311	
	US 5300564	

DOCUMENT TYPE: Utility
FILE SEGMENT: CHEMICAL
GRANTED
ENTRY DATE: Entered STN: 27 Oct 1998
Last Updated on STN: 8 Jul 2002

NUMBER OF CLAIMS: 11
GRAPHICS INFORMATION: 1 Drawing Sheet(s), 1 Figure(s).

AB A sol-gel glass doped with one or more reagent that provides chemical interactions with diffusible solutes or components in an adjacent liquid or gas phase. The reagent(s), the solutes or the components can be any organic or inorganic compounds or materials of biological origin, including enzymes. The doped sol-gel glass in various forms is useful as an analytical test, chromatographic medium, sensor, catalyst or biocatalyst, electrode or enzyme electrode, and other detection devices.

CLMN 11
GI 1 Drawing Sheet(s), 1 Figure(s).

L6 ANSWER 4 OF 7 IFIPAT COPYRIGHT 2008 IFI on STN
AN 02864303 IFIPAT;IFIUDB;IFICDB <<LOGINID::20080306>>
TITLE: DOPED SOL-GEL GLASSES FOR OBTAINING CHEMICAL INTERACTIONS
INVENTOR(S): Avnir, David, Jerusalem, IL
Braun, Sergei, Jerusalem, IL
Ottolenghi, Michael, Jerusalem, IL

	Zusman, Rivka, Jerusalem, IL
PATENT ASSIGNEE(S):	Yissum, Research Development Company of the Hebrew University of Jerusalem, Israel, Jerusalem, IL
PRIMARY EXAMINER:	Lovering, Richard D
AGENT:	Lowe, Price, LeBlanc & Becker

	NUMBER	PK	DATE
PATENT INFORMATION:	US 5650311	A	19970722
	(CITED IN 004 LATER PATENTS)		
APPLICATION INFORMATION:	US 1994-266441		19940628
EXPIRATION DATE:	22 Jul 2014		

	APPLN. NUMBER	DATE	GRANTED PATENT NO. OR STATUS
CONTINUATION OF:	US 1992-937259	19920831	ABANDONED
DIVISION OF:	US 1991-637873	19910108	5300564

	NUMBER	DATE
PRIORITY APPLN. INFO.:	IL 1990-93134	19900123
FAMILY INFORMATION:	US 5650311	19970722
	US 5300564	
DOCUMENT TYPE:	Utility	
	CERTIFICATE OF CORRECTION	
CORRECTION DATE:	30 Jun 1998	
FILE SEGMENT:	CHEMICAL	
	GRANTED	
ENTRY DATE:	Entered STN: 14 Aug 1997	
	Last Updated on STN: 18 Nov 1997	

NUMBER OF CLAIMS:	9
GRAPHICS INFORMATION:	1 Drawing Sheet(s), 1 Figure(s).

AB A metod is proposed of obtaining a chemical interaction between at least one reagent trapped in sol-gel glass by doping it with the reagent(s), and diffusible solutes or components in an adjacent liquid or gas phase. The reagents, the solutes or the components can be any organic or inorganic compounds or materials of biological origins including enzymes. The doped sol-gel glass in various forms may be useful as analytical test, chromatographic medium, sensor, catalyst or biocatalyst, electrode or enzyme electrode, or other detection device.

CLMN 9

GI 1 Drawing Sheet(s), 1 Figure(s).

L6 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER:	2002:670145 CAPLUS <<LOGINID::20080306>>
DOCUMENT NUMBER:	138:162594
TITLE:	Determination of heavy metal ions using conductometric biosensor based on sol-gel-immobilized urease
AUTHOR(S):	Lee, Sang-Mok; Lee, Won-Yong
CORPORATE SOURCE:	Department of Chemistry, Yonsei University, Seoul, 120-749, S. Korea
SOURCE:	Bulletin of the Korean Chemical Society (2002), 23(8), 1169-1172
	CODEN: BKCSDE; ISSN: 0253-2964
PUBLISHER:	Korean Chemical Society
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB The anal. characteristics of the conductometric biosensor, which is based

on sol-gel-immobilized-urease, for the determination of heavy-metal ions were examined This durable conductometric biosensor can be advantageously used in harsh conditions such as environmental monitoring. The heavy metal ions used in the urease inactivation study were prepared from Hg(NO3)2, Cu(NO3)2, Cd(NO3)2, and Pb(NO3)2. Sol-gel-immobilized-urease biosensor on a thick-film IDA electrode can be used as a reliable tool for the determination of heavy-metal ions in liquid samples. The present biosensor exhibits several advantages; easy production of the sensor, low cost, good sensor-to-sensor reproducibility, no chemical modification of the substrate or enzyme for the enzyme immobilization process, and further possibility to control of the biosensor performance by changing the alkoxide/water ratio in the stock sol-gel solution in the construction of the biosensor.
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:48059 CAPLUS <<LOGINID::20080306>>
DOCUMENT NUMBER: 132:104888
TITLE: Microfabricated conductometric urea biosensor based on sol-gel immobilized urease
AUTHOR(S): Lee, Won-Yong; Lee, Kang Shin; Kim, Tae-Han; Shin, Min-Chol; Park, Je-Kyun
CORPORATE SOURCE: Devices Materials Lab., LG Corporate Institute Technology, Seoul, 137724, S. Korea
SOURCE: Electroanalysis (2000), 12(1), 78-82
CODEN: ELANEU; ISSN: 1040-0397
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A conductometric biosensor was constructed with a sol-gel immobilized urease on a microfabricated interdigitated array (IDA) gold electrode. Tetramethoxysilane (TMOS) was used as a sol-gel precursor for the immobilization of the urease and the performance of the resulting urea biosensor was controlled through the water content in the acid-catalyzed hydrolysis of the sol-gel stock solution The sol-gel-derived urea biosensor showed relatively wide dynamic range of 0.2-50 mM in 5 mM imidazole-HCl buffer at pH 7.5. Furthermore, the urea biosensor exhibited good sensor-to-sensor reproducibility (6.5%) and storage stability (50% of its original activity retained after 3 wk) when stored in 5 mM imidazole-HCl buffer at 4°. The urea biosensor was successfully applied for the urea determination in urine sample by employing the differential measurement format consisting of an active IDA conductometric sensor containing sol-gel-immobilized urease and a reference IDA conductometric sensor containing bovine serum albumin layer instead of the urease.
REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 7 OF 7 BIOTECHDS COPYRIGHT 2008 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2003-13212 BIOTECHDS <<LOGINID::20080306>>
TITLE: Preparing nucleic acid conjugates with synthetic binding units, by synthesizing conjugates on solid support using monomer/oligomer units, treating support with alkylamine solution, and treating support with hydrazine;
bioarray e.g. DNA array, RNA array, locked nucleic acid array, peptide nucleic acid array, aptamer array and aptazyme array construction
AUTHOR: SCHWEITZER M; ANDERSON R; FIECHTNER M; MUELLER-IBELER J; RADDATZ S; BRUECHER C; WINDHAB N; ORWICK J; SCHNEIDER E; PIGNOT M; KIENLE S

PATENT ASSIGNEE: NANOGEN RECOGNOMICS GMBH
PATENT INFO: WO 2003008638 30 Jan 2003
APPLICATION INFO: WO 2002-EP1532 14 Feb 2002
PRIORITY INFO: US 2001-910469 19 Jul 2001; US 2001-910469 19 Jul 2001
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2003-300432 [29]
AN 2003-13212 BIOTECHDS <<LOGINID::20080306>>
AB DERWENT ABSTRACT:

NOVELTY - Improved method (M) for preparing nucleic acid conjugates (C) with synthetic binding units involves: (i) synthesizing (C) on a solid support phase using monomer or oligomer units, where the units are beta-cyanoethyl-protected on at least one phosphorus of the units; (ii) treating support with a solution of an alkylamine in an inert solvent; and (iii) treating the support with hydrazine to cleave off and deprotect (C).

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) a supermolecular construct (I) comprising at least one synthetic address unit (SAU) attached to a support material comprising an array of discrete locations, where the same SAU is attached to at least two predetermined locations on the support material, and at least two conjugates comprising synthetic binding unit (SBU) and a nucleic acid (NA), where at least two of the conjugates have the same SBU and different NAs, where the SBU of the conjugates form a synthetic binding system unit (SBS) with the SAU at the two predetermined locations, and immobilize each of the two different NAs at a different location; (2) a conjugate (II) with the general formula (NA)-(SBU), where each NA is linked to at least one SBU by a linker X, and X is selected from groups of formulae (F1), (F2), (F3), (F4) and (F5); (3) a conjugate (III) with a general formula (NA)n-(SBU)m; (4) a supermolecular construct (IV) comprising at least one of (II) or (III) and at least one SAU which is specifically associated with at least one SBU of the conjugate to form a SBS, where the SAU is attached to a support material (SM); (5) a library (V) comprising at least two conjugates such as (II) and/or (III); (6) a unit (VI) of a SBS selected from SBU and SAU, comprising an oligomer of monomeric units, where the monomeric units have a group of formula -R6(R7)- (F7), and the monomeric units are linearly arranged according to the formula (As)-(J)-(As) or (As)-(J)-(As)-(J')-(As); and(7) a kit for immobilizing biomolecules comprising at least two SBUs or SAUs of (VI), where the SBUs or SAUs are orthogonal. Y1 and Y2 = OH, SH, NH2 or CH3; G = O or S; L1 and L2 = linkers such as a covalent bond, and a linker chain moiety comprising an optionally saturated, optionally branched, optionally substituted, chain of 1-60C and 0-40 heteroatoms such as N, O and S; V1 and V2 = -CH2- or -NHCO-; R1 and R2 = H or OH; R5 = nitrogen heterocyclic moiety; R6 = backbone moiety which connects the monomeric unit to the oligomer; R7 = specific recognition moiety comprising a nitrogen heterocycle moiety; s = 0-10; A = any monomeric unit as is used for synthesizing SBU; and J, J' = a sequence of recognition moieties (RS), and are selected from p-RNA-polynucleotides, p-DNA-polynucleotides and CNA-polynucleotides, a group orthogonal sequences, sequences given in the specification. NA = a nucleic acid; SBU = a synthetic binding unit; n, m = 1-6; n+m = greater than 2. Each NA is linked to at least one SBU.

BIOTECHNOLOGY - Preferred Construct: In (I), the SBU and the SAU each comprise an at least partially complementary sequence of monomeric units which non-covalently associate with one another in a sequence-dependent manner. The SAU comprises, independently of the SBU, an oligomer selected from p-RNAs, p-DNAs and CNAs. At least one discreet location has a known mixture of SAUs attached at that location. The support material comprises a material selected from silicon, silicon dioxide, silicon nitride, controlled porosity glass, metal, inorganic

sol-gels, and hydrogels. The support material is a permeation layer over an electrode of an active electronic array. The SAUs are attached to the support material through a biotin/streptavidin interaction or through at least one covalent bond. The covalent bond is formed by reacting a hydrazide group on SAU with a functional group on the support. The SBUs of the conjugate are oligomers comprised of monomeric units, where the monomeric units have the formula F7. The NA of the conjugates are selected from DNA and RNA, chemically modified nucleic acids, phosphorothioate nucleic acids, phosphorodithioate nucleic acids, methylphosphonate nucleic acids, 2'-O-methyl RNA, 2'-fluoro RNA, peptide nucleic acids (PNA), locked nucleic acids (LNA), an aptamer and an aptazyme. The conjugates further comprise at least one labeling moiety selected from fluorescent moieties, quencher moieties, visible dye moieties, radioactive moieties, chemiluminescent moieties, biotin moieties, hapten moieties, microparticles, paramagnetic microparticles, and enzymatic labeling moieties.

USE - (M) is useful for preparing nucleic acid conjugates with synthetic binding units. (II) is useful for producing an array of immobilized nucleic acids on an active location array device comprising a number of activatable locations on a support material, by activating a first set L1 of locations on the active array device, where at least some of the activated locations comprise a predetermined SAU or set of SAUs attached at the locations, and where the activation of the locations creates a condition favorable to the binding of the SAUs to SBUs, contacting the activated set of locations with a first set C1 of SBU-NA conjugates, where at least some of the SBUs in the set of conjugates are capable of specifically binding to at least some of the SAUs attached at the activated locations, removing the unbound conjugates, and repeating the above mentioned steps M number of times, activating set L(M+1) of locations, and contacting them with set C(M+1) of conjugates, where M at least 1. (II) or (III) is useful for producing a set of immobilized nucleic acids on a support material, by providing a support material, where SAU are attached at predetermined positions on the support, and contacting (II) or (III), where (II) or (III) comprise at least one SBU which specifically binds to at least one SAU on the support, with the support under conditions suitable for the association of SBU's and SAU's to form SBS's. (II) is useful for enzymatically modifying a nucleic acid selected from a target nucleic acid and the nucleic acid of a conjugate comprising at least one NA and at least one SBU, utilizing the nucleic acid of the conjugate as a substrate, by contacting the conjugate with at least one enzyme which utilizes naturally occurring nucleic acids as a substrate, and with other reagents necessary for the action of the enzyme, and incubating the mixture obtained under conditions suitable for the functioning of the enzyme for a period of time sufficient to effect the modification of the nucleic acid (all claimed). (II) or (III) is useful for sorting and immobilizing nucleic acids on support material, in active electronic arrays system to produce novel array constructs useful in various nucleic acid assay formats, as substrates for various enzymatic reactions, including nucleic acid amplification reactions, or to sort relatively complex mixtures of nucleic acids to predetermined locations on a support for facile analysis or further use in nucleic acid based biological assays.

ADVANTAGE - (I) enables efficient and specific sorting of relatively complex mixtures of nucleic acids to predetermined locations on a support. (I) allows significant time reduction and simplification of method of immobilization of different nucleic acids on an array .

EXAMPLE - Synthesis of conjugates of nucleic acids and synthetic binding systems was as follows: Conjugates of 4'pRNA2'-5'-DNA3' was

synthesized. The synthesis was begun with a standard solid phase DNA synthesis in the 3'-5' direction to produce the desired DNA sequence. If a linking group or branching group was desired, the appropriate synthesis building blocks were coupled to the 5' end of the product. If the DNA was directly linked to pRNA through a phosphate, no linker phosphoramide was used. Next, the monomer building blocks of pRNA were coupled so that a synthetic binding unit (SBU) binding address of the desired length and sequence was obtained. If a labeled conjugate was desired, marker phosphoramidites were coupled to the conjugate in an optional last step, or utilized as an initial coupled reagent in the synthesis. Here, the fluorescent dye phosphoramidites Cy3 and Cy5 were useful, but any other suitable phosphoramidite dyes derivatives known from DNA synthesis could also be used. The conjugate was worked up, deprotected, isolated and purified. Analogously, it was possible to prepare conjugates of pRNA and modified nucleic acids (e.g. 2-'O-methyl RNA). For this, 2'-O-methylphosphoramidites were coupled after the pRNA. The nucleic acid was also occasionally phosphorylated at its 5' end. For this purpose, building blocks for introducing phosphates were used. Applying the general protocol led to conjugates (bold = pRNA; italics = DNA) such as: IL4RP102a: 4'TCCTGCATTC2'-5'GCATAGAGGCAGAATAAGAGG3', or IL4RP103a: 4'CTCTACGTCT2'-5'GCATAGAGGCAGAATAACAGG3'. (232 pages)